REMARKS

Claims 1-21 are pending in the present application. Claims 1-10 are rejected under 35 USC §112. Claims 1, 6-7 and 9-21 are rejected under 35 USC §103(a). Claims 11-21 are rejected under the judicially created doctrine of obviousness-type double patenting. Applicants respectfully request reconsideration of the application, withdrawal of all rejections, and allowance of the application in view of the amendments and remarks below.

The Invention

The present invention provides novel condensation drug aerosols and methods for producing such aerosols. These condensations aerosols have little or no pyrolysis degradation products. The unique method for generating or producing such aerosols employs rapid vaporization of the drug to minimize drug degradation during the process. These vaporized drugs are subsequently condensed to form particles of a desirable particle size for inhalation. These aerosols are especially useful in the treatment of acute or chronic conditions wherein rapid onset of treatment is desirable.

The Amendments to the Specification

The specification has been amended, at paragraphs **[0108]**, to note a calculated thickness of a zaleplon thin layer, on a 24 cm^2 aluminum foil solid support, of about 2.3 microns, based on an assumed drug density of 1g/cc.

The specification has been amended, at paragraph **[0109]**, to note a calculated thickness of a zolpidem thin layer, on a 24 cm^2 aluminum foil solid support, of about 2.3 microns, based on an assumed drug density of 1g/cc.

The specification has been amended, at paragraph **[0110]**, to note a calculated thickness of a zopiclone thin layer, on a 24 cm^2 aluminum foil solid support, of about 1.5 microns, based on an assumed drug density of 1g/cc.

The specification has been amended, at paragraph **[0111]**, to note a calculated thickness of a zolpidem thin layer, on a 24 cm^2 aluminum foil solid support, of about 4.4 microns, based on an assumed drug density of 1g/cc.

The specification has been amended, at paragraph **[0113]**, to note a calculated thickness of a zolpidem thin layer, on a 24 cm^2 aluminum foil solid support, of about 3.4 microns, based on an assumed drug density of 1g/cc.

The amendments to the specification at paragraphs **[0108]-[0111]** and **[0113]** parallel the

amendments that were made with respect to the parent U.S. patent application Serial No. 10/150,857, now U.S. Patent No. 6,716,415.

It is well-established in the case law that amendatory material is not new matter where it is concerned with an inherent characteristic of an illustrative product of an invention already sufficiently identified in the original patent disclosure. (*In re Nathan, Hogg, and Schneider*, 140 USPQ 601 (CCPA, 1964); In *In re Reynolds*, 170 USPQ 94 (CCPA 1971) the CCPA cited with approval the following holding from *Technicon Instruments Corp. v. Coleman Instruments, Inc.*, 255 F. Supp. 630, 150 USPQ 227 (N.D. Ill. 1966):

> By disclosing in a patent application a device that inherently performs a function, operates according to a theory, or has an advantage, a patent applicant necessarily discloses that function, theory, or advantage even though he says nothing concerning it. The application may be amended to recite the function, theory, or advantage without introducing prohibited new matter.

This principle has been endorsed by the CAFC, e.g., in *Kennecott Corp., v. Kyocera Int'l l Inc.*, 835 F. 2d. 1419, 5 USPQ2d 1194 (Fed. Cir. 1987).

The amendatory material regarding the assumed density of the drugs is already stated in the specification, e.g., see paragraph **[0111]** which states " . . . multiplied by the density of the drug (taken to be 1 g/cm^3)." Additionally, the thickness of the coating would be readily derivable by a person skilled in the art of the claimed invention by multiplying the mass of the material by its density and then dividing this by the surface area over which it is coated. As stated above information regarding the density is readily available from the specification and other recognized sources (e.g., the CRC Handbook of Chemistry and Physics, the Aldrich Chemical Catalog, etc.) and can be assumed to about 1g/cc. The drug masses and substrate areas are also disclosed in the specification. This information is all that is needed for one to calculate the thickness.

Thus, no new matter is introduced by these amendments to the specification. The Examiner is respectfully requested to enter the amendments to the specification.

The Amendments to the Claims

Without prejudice to the Applicants' rights to present claims of equal scope in a timely filed continuing application, to expedite prosecution and issuance of the application, the Applicants have amended Claims 1-3, 5, 6, 11, 13 and 15-21 and cancelled Claims 4, 7-10 12 and 14. The Applicants also have presented new Claims 22-41. The amended claims and the new claims are supported by the specification (see below for examples of such support).

Claim	Examples of Support in the Specification
Claim 1	Paragraphs 0004, 0037, 0040, 0043; Examples 1-5
Claim 2	Paragraph 0043
Claim 3	Paragraph 0051
Claim 5	Paragraph 0049
Claim 6	Paragraph 0042
Claim 11	Paragraphs 0004, 0037, 0040, 0043; Examples 1-5
Claim 13	Paragraphs 0004, 0037, 0040, 0043, 0054, 0055; Examples 1-5
Claim 15	Paragraphs 0004, 0037, 0040, 0043, 0054, 0055, 0090, 0091; Examples 1-5; Figure 1
Claim 16	Paragraph 0089
Claim 17	Paragraph 0089
Claim 18	Paragraph 0089
Claim 19	Paragraph 0085
Claim 20	Paragraph 0051
Claim 21	Paragraphs 0054, 0055
Claim 22	Paragraphs 0050
Claim 23	Paragraphs 0050
Claim 24	Paragraphs 0050
Claim 25	Paragraphs 0001 [incorporates by reference U.S. provisional application Ser. No. 60/317,479 (see e.g., page 30, lines 25-27)], 0043
Claim 26	As recited above for Claim 25
Claim 27	Examples 1-5
Claim 28	Paragraph 0037
Claim 29	Paragraph 0037
Claim 30	Paragraph 0037
Claim 31	Paragraph 0043
Claim 32	Paragraphs 0001 [incorporates by reference U.S. provisional application Ser. No. 60/317,479 (see e.g., page 30, lines 25-27)], 0043
Claim 33	As recited above for Claim 32
Claim 34	Examples 1-5
Claim 35	Paragraph 0055
Claim 36	Paragraph 0055
Claim 37	Paragraph 0055
Claim 38	Paragraph 0085
Claim 39	Paragraph 0085
Claim 40	Paragraph 0088
Claim 41	Paragraph 0086

The amendments to the claims do not introduce new matter. Applicants respectfully submit that the amendments to the claims put the case in condition for allowance. The Examiner is respectfully requested to enter the amendments to the claims and allow all amended claims.

The Rejection under 35 U.S.C. §112

The Examiner rejected Claims 1-10 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "by the patient of the formation of, and delivery of, the condensation aerosol" in Claims 1 and 7 was found to be unclear and redundant. Claim 1 has been amended to eliminate this phrase. Claim 7 has been cancelled.

The Rejection under 35 U.S.C. §103(a)

The Examiner rejected Claims 1, 6-7 and 9-21 under 35 U.S.C. §103(a) as being unpatentable over Bartus et al. (6,514,482) in view of Faithfull et al. (6,041,777). In support of this rejection, the Office Action states that "Bartus teaches a method of pulmonary delivery of a medicament, which includes administering . . . particles . . . , where the particles preferably have an aerodynamic diameter between about 1 and 5 μm." Office Action at 2-3. The Office Action further states that Bartus discloses medicaments containing from 1 to about 90 weight percent of drugs, including zolpidem, zaleplon, temezepam, etc., that are delivered via a dry powder inhaler, metered dose inhaler, nebulizer or instillation techniques. *Id.* at 3.

The Office Action states that Bartus lacks "teachings on producing condensation aerosol and also lacks specific disclosure on the presence of less than 5% degradation products" *Id.* at 3. The Office Action states in summary that Faithfull teaches methods and apparatus for closed-circuit ventilation therapy, including the use of nebulizers to provide fluorochemicals and/or pharmaceutical agents, heated above body temperature, to a ventilating gas in the form of a vapor and that this is accomplished by spraying or contacting a wetted surface or wick with the gas to form droplets. *Id.* at 3-4.

The Office Action states that it "would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method of delivering a medicament to a patient's respiratory tract of Bartus, by adding the steps of heating the composition and having patient inhale the condensates, because of the disclosed benefits of such a method, including minimized trauma to the lungs and a better resolution of pulmonary and systemic disorders, as taught by Faithfull." *Id.* at 4.

Applicants respectfully disagree in view of the elements of the pending claims and the disclosures of Bartus and Faithfull. Bartus fails to teach or disclose a condensation aerosol. Rather Bartus is directed to a method of delivering low tap density particles for the treatment of CNS disorders and in particular, Parkinson's disease, via dry power inhalers or metered dose inhalers. Nowhere does Bartus disclose or suggest an aerosol particle formed as a condensate of a vaporized drug, nor the advantages obtained by such a condensate aerosol. Additionally, Bartus lacks teachings on heating the composition. Dry powder

inhalers, metered dose inhalers, nebulizers or instillation techniques do not vaporize the drug and then form a condensate of the drug. Additionally, in Bartus there is no disclosure of how one would form such particles of an antiparkinsonian drug or any other drug compound to generate an aerosol characterized by less than 10% drug degradation products, or how to obtain aerosols having a MMAD of less than 5 microns when vaporizing the drug. Nor does Bartus disclose heating a thin layer, containing the drug, on a solid support. These elements, which are not taught in Bartus, are required by independent Claims 1, 11 and 13.

Faithfull does not cure these deficiencies or make obvious in view of Bartus how to accomplish these tasks. Faithfull does not disclose or teach a condensation particle or aerosol as defined by the Applicants' claims or how to make such an aerosol. Faithfull discloses the use of a warmed fluorochemical as a solvent for delivering the active compound "oxygen" to the lungs of the patient using a ventilation system. The active or therapeutic compound or drug in Faithfull is not vaporized and subsequently condensed into aerosol particles, as is set forth in Claims 1, 11 and 13 of the present application. Moreover, there is no teaching in Faithfull of drawing air through an enclosure being effective to condense a vapor to form a condensation aerosol, as required in Claim 15. Rather, Faithfull teaches away from such a condensation aerosol, as oxygen gas is already being passed through the system described by Faithfull and no condensation aerosol is formed. Instead, Faithfull requires the use of a wetted surface or wick to get the fluorochemical (solvent) to form a droplet. Moreover, as is stated in the Office Action, the fluorochemical in the Faithfull reference, unlike the present invention, is being delivered to the lung as a vapor and not an aerosol. See Office Action at 4 ("As the fluorochemical **vapor** cools in the body it is deposited on the pulmonary surfaces" (emphasis added)). Faithfull does not disclose how to make a condensation aerosol having the purity disclosed in the present application, or how to obtain MMAD sizes of less than 5 microns for condensation aerosols. Nor does Faithfull disclose heating a thin layer, containing the drug, on a solid support.

The Office Action suggests that condensates by their nature have a high percentage of purity of the drug and less degradation products. Applicants respectfully disagree. The mere fact that an aerosol is formed by condensation does not mean that the aerosol will have a high percentage of drug and less degradation products.

According to the MPEP § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations." Obviousness cannot be established by combining teachings in the prior art, absent some

teaching or suggestion in the prior art that the combination be made (*In re Stencel* 828 F. 2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987); *In re Newell* 891 F. 2d 899, 13 USPQ2d 1248 (Fed. Cir. 1989)).

Faithfull does not cure the deficiencies of Bartus. Accordingly, the Office Action fails to establish even a *prima facie* case of obviousness as each and every element of the invention is not taught or disclosed by these references. Moreover, there would be no motivation to combine the references to achieve the presently claimed invention. Even if the cited references were combined, the claimed invention would not result because neither Bartus nor Faithfull is directed to heating a thin layer containing a drug, on a solid support, or to forming condensation aerosols suitable for inhalation that are characterized by less than 10% drug degradation products and an MMAD of less than 5 microns.

Claims 2, 3, 5, 6 and 22-27 which depend from Claim 1 patentably define over Bartus and Faithfull for the same reasons as Claim 1. Claims 28-30 which depend from Claim 11 patentably define over Bartus and Faithfull for the same reasons as Claim 11. Claims 15-21 and 31-41 which depend from Claim 13 patentably define over Bartus and Faithfull for the same reasons as Claim 13.

Finally, the Examiner rejected Claims 1, 6-7 and 9-21 under 35 U.S.C. 103(a) as being unpatentable over Bartus et al. (6,514,482) in view of Byron et al. (20040016427 A1). Office Action at 4. The Office Action states that Bartus "lacks disclosure on condensation aerosols and the devices for producing condensates involved in the method of therapy," but that "Byron et al. disclose a method and apparatus for generating an aerosol . . . formed by supplying a material in liquid form to a tube and heating the tube such that the material volatizes and expands out of an open end of the tube." *Id.* at 4-5. The Office Action goes on to state that the volatized material combines with ambient air such that volatized material condenses to form the aerosol and that the aerosols are intended for inhalation and typically have a mass median particle diameter of less than 2 microns. Thus according to the Office Action, it would have been obvious to take the device of Byron and use it to deliver the aerosolized composition of Bartus to a subject's respiratory tract as it would be desirable to provide an aerosol delivery article capable of making small particles without exposure to significant heat or high temperatures. *Id.* at 5.

Applicants respectfully disagree. One of skill in the art seeking to prepare and administer aerosolized compositions for delivery to a subject's respiratory tract without exposure to significant heating or high temperatures would not have to look beyond the disclosure of Bartus. Moreover, Bartus does not teach that small particles are desirable. To the contrary, Bartus states that larger, low density particles aerosolize more efficiently and avoid phagocytic engulfment by alveolar macrophages more effectively than smaller, denser aerosol particles. Bartus col. 13, lines 61-64.

> "The aerodynamic diameter can be calculated to provide for maximum deposition within the lungs. Previously this was achieved by the use of very small particles of less than about five microns in diameter, preferably between about one to about three microns, which are then subject

to phagocytosis. Selection of particles which have a larger diameter, but which are sufficiently light (hence the characterization "aerodynamically light"), results in an equivalent delivery to the lungs, but the larger size particles are not phagocytosed. Improved delivery can be obtained by using particles with a rough or uneven surface relative to those with a smooth surface" (Bartus col. 13, line 65 to col. 14, line 7).

As pointed out in the Office Action, the aerosols generated by the device of Byron et al. typically have a mass median particle diameter of less than 2 microns, while Bartus teaches that the preferred size range of particles is at least about 5 microns, preferably between about 5 microns and 30 microns. See, e.g., Bartus at col. 12, lines 60-66; col. 14, lines 12-14. Thus, Bartus teaches away from delivering its compositions using the device of Byron et al.

Moreover, one of skill in the art would not have a reasonable expectation that the device of Byron et al. would successfully form condensation aerosols suitable for inhalation that are characterized by less than 10% drug degradation products and an MMAD of less than 5 microns from the compositions of Bartus. For instance, under the method of Byron et al., the compositions of Bartus ("solid component") would have to be put into liquid form by combining with a "liquid component." Byron et al., paragraph [0076]. However, Byron et al. fails to provide specific guidelines for selecting an appropriate "liquid component" for a given drug ("solid component") or for predicting what effect heating the mixture will have on the solid component. This is further complicated when the solid component contains one or more additional component in addition to the drug, such as the surfactants, phospholipids, amino acids, etc., taught in Bartus. Bartus, col. 8, lines 42 to col. 11, line 53.

Finally, these references do not teach or suggest all of the elements of independent Claims 1, 11 and 13. Like Bartus, Byron et al. lacks specific disclosure on the presence of less than 10% degradation products. Furthermore, neither Bartus nor Byron et al. describes heating a thin layer, containing the drug, on a solid support.

Thus, these references singly or in combination do not teach or suggest all the claim elements, but rather teach away from the claimed invention. Accordingly, the Office Action fails to establish even a *prima facie* case of obviousness. Moreover for the same reason, there would be no motivation to combine the references to achieve the presently claimed invention, nor is it seen how the combination of the references would achieve the presently claimed invention. Claims 2, 3, 5, 6 and 22-27 which depend from Claim 1 are not obvious for the same reasons as Claim 1. Claims 28-30 which depend from Claim 11 are not obvious for the same reasons as Claim 11. Claims 15-21 and 31-41 which depend from Claim 13 are not obvious for the same reasons as Claim 13.

Accordingly, and in light of the foregoing arguments, the Applicants respectfully submit that these amendments put the case in condition for allowance and request that the Examiner reconsider and withdraw all rejections based on 35 U.S.C §103.

Double Patenting

Claims 11-21 were rejected under the judicially created doctrine of obviousness-type double patent as being unpatentable over claims of U.S. Patent No. 6,716,415 B2, as these claims are "either anticipated by, or would have been obvious over, the reference claims." Office Action at 6. Also, Claims 11-21 were provisionally rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application Nos. 10/766,149 and 10/718,982. *Id.* at 6-7.

Applicants have filed with this response Terminal Disclaimers with regard to U.S. Patent No. 6,716,415 B2 and copending Application Nos. 10/766,149 and 10/718,982. Applicants believe that this addresses the Examiner's concerns and respectfully request reconsideration of the application, withdrawal of all rejections, and allowance of the application in view of these actions and remarks.

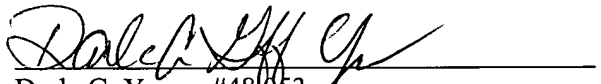
Conclusion

The Applicants appreciate the Examiner's careful and thorough review of the application and submit that the Examiner's concerns have been addressed by the amendments and remarks above. The Applicants accordingly request the Examiner to withdraw all rejections and allow the application. In the event the Examiner believes a telephonic discussion would expedite allowance or help to resolve outstanding issues, prosecution of the application, then the Examiner is invited to call the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

Date: September 22, 2005



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